"A STUDY OF BIOMARKERS IN RELATION TO THE RISK OF METABOLIC SYNDROME AND ITS ASSOCIATED COMPLICATIONS IN INDIAN OVERWEIGHT AND OBESE POPULATION"

SYNOPSIS

Of the Thesis submitted for the award of

Degree of

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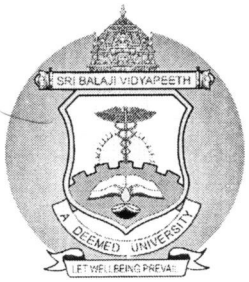
In

BIOCHEMISTRY

(Faculty of Medicine)

Submitted to



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OCTOBER, 2024

CERTIFICATE

We certify that the **Synopsis** of the **Thesis** entitled **"A STUDY OF BIOMARKERS IN RELATION TO THE RISK OF METABOLIC SYNDROME AND ITS ASSOCIATED COMPLICATIONS IN INDIAN OVERWEIGHT AND OBESE POPULATION"** submitted for the Degree of **Doctor of Philosophy in Biochemistry (Faculty of Medicine)**, is a Record work carried out by **Ms. Sruti.E** at the Department of Biochemistry, Tomo Riba Institute of Health & Medical Sciences during the period from September 2020 to September 2024 under our guidance and supervision. This work is original and has not been submitted elsewhere for the award of any Degree, Diploma, Associateship, Fellowship or other similar titles.

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INTRODUCTION:

India is undergoing a rapid epidemiological transition from underweight to overweight/obese population. Reports from different parts of India suggested that the prevalence of men and women living with overweight/obesity were observed to be 38.4% and 36.2% respectively. The Indian National Family Health Survey -4 reported that in the 10 years period from 2005 and 2006 to 2015 and 2016, obesity among women between the ages of 15 and 49 years has increased from 13% to 21% during the same period obesity among men between the ages of 15 and 49 years has increased from 9.3% to 19%.

Recent reports suggest that obesity is one of the most neglected public health problem and it is associated with unemployment, social disadvantages and reduced socioeconomic productivity. Metabolic syndrome has gained significant importance recently due to exponential increase in obesity worldwide. The prevalence of metabolic syndrome often corresponds with the prevalence of obesity. The overall prevalence of metabolic syndrome in Indian adult population was 30% (1).

Metabolic Syndrome:

Metabolic syndrome (MetS) also labeled as 'insulin resistance syndrome', 'syndrome X', 'hypertriglyceridemic waist', and 'the deadly quartet', is a cluster of metabolic abnormalities that includes hypertension, central obesity, insulin resistance, and atherogenic dyslipidemia. According to IDF Criteria metabolic syndrome is classified as: having central obesity (Waist circumference >90 cm in men, >80 cm in women) along with two of the following factors. 1. TG ≥150 mg/dl 2. HDL levels < 40mg/dl in men or < 50 mg/dl in women 3. B.P ≥130/85 mm Hg 4. Fasting blood glucose > 100 mg/dl.

Risk factors for Metabolic Syndrome:

The two major factors which are universally accepted in the causation of MetS are insulin resistance and central obesity. In addition, certain genetic/progenetic factors, physical

inactivity, advancing age, female gender, and pro-inflammatory state may also have a contributory effect, their role being variable and depending on the ethnic group.

Insulin resistance: insulin resistance occurs when the sensitivity of cells in the body, to the action of insulin, starts declining; eventually, they become resistant to the action of insulin; due to development of resistance to insulin action, peripheral utilization of glucose is adversely affected, and consequently a larger amount of glucose remains in the blood; this triggers the need for more and more insulin to be produced and secreted into the blood, in an attempt to utilize the increased quantity of retained blood glucose, thus resulting in hyperinsulinemia; such production of increasing amounts of insulin eventually wears out the beta cells; once the beta cells are no longer able to produce enough insulin, a person becomes hyperglycemic, resulting in Type 2 Diabetes Mellitus (T2DM) .However, even before the state of T2DM occurs, much damage would have already occurred to the body, including an increase in triglycerides, which further impairs insulin sensitivity.

Central obesity: generalized obesity is a well-documented risk factor for T2DM and Ischemic Heart Disease. However, more than generalized obesity as seen in the form of raised Body Mass Index (BMI), it is the "central obesity" that occurs due to excessive deposition of fat in the intra-abdominal compartment (also known as visceral/peritoneal compartment), which is a much stronger risk factor for development of MetS. Central Obesity is quite easily and effectively measured by an increase in waist circumference (WC) or Waist Hip Ratio (WHR).

Pathophysiology of Metabolic Syndrome:

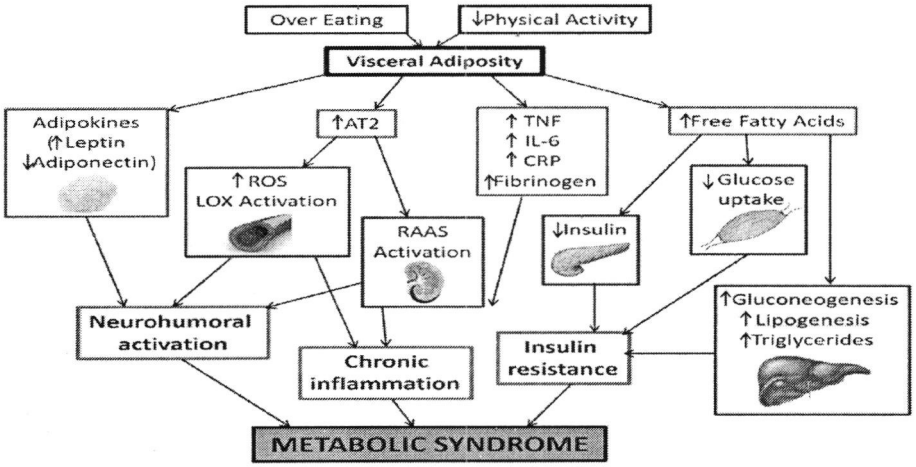

Figure 1. Pathophysiological mechanisms in metabolic syndrome (2)
(AT-Adipose Tissue, TNF-Tumor Necrosis Factor, IL-Interleukin, CRP-C-Reactive Protein, ROS- Reactive Oxygen Species, RAAS- Renin-Angiotensin-Aldosterone System)

ADIPOKINES AND HEPATOKINE:

Accumulating evidence indicate that adipokines and hepatokines have been a centre of appreciation and interest. They are biologically active molecules causing pleiotropic effects. They assist in angiogenesis, adipose tissue metabolism and inflammation and modulate tissue sensitivity for insulin.

Chemerin:

Chemerin is a newly discovered adipocytokine firstly identified in 1997 is encoded by Retinoic acid receptor responder 2 (RARRES2) and secreted as a 143 amino acid precursor with low biological activity to become active further extracellular C-Terminal processing is needed. Chemerin a well characterized chemoattractant secreted mainly from mature adipocytes and highly expressed in the adipose tissue. Chemerin had a critical role in the regulation of immune response, adipocyte differentiation and metabolic homeostasis via its binding to G protein chemerin receptors. The medical literature has pointed out that chemerin may link obesity and inflammation since it is a proinflammatory cytokine that results and activates immune cells & contributes to inflammation by promoting macrophage adhesion to

vascular cell adhesion molecule – 1 (VCAM-1) and fibronectin. Although previous reports and biological plausibility have indicated that serum chemerin levels associated with parameters of the metabolic syndrome and it is involved in the pathophysiology of type 2 diabetes & changes of chemerin precede the onset of type 2 diabetes. However previous studies have produced mixed results some revealed opposite or no association. Chemerin may also be a novel predicting factor for cardiovascular events and cancer in patients with metabolic syndrome independent of standard risk factors (3).

Visfatin:

Visfatin is a recently discovered adipocytokine with 55-kDa protein consisting of 491 amino acids was previously called pre-β cell colony enhancing factor (PBEF). Visfatin is secreted by macrophages (CD 14^{+}) in visceral adipose tissue induced by hypoxia under hypoxic conditions, hydroxylase processes are rendered inactive consequently hypoxia – inducible factor – 1a is stabilized and moves into the nucleus where it binds to hypoxia response elements within target genes and initiates the transcription of visfatin. Visfatin is synthesized and released by inflammatory cells in adipose tissue as well as adipocytes. It has the ability to activate human leukocytes. It induces the synthesis of proinflammatory cytokines and adhesion molecules, regulates the maturation of leukocytes B and inhibits apoptosis of neutrophils. Recent studies have indicated that visfatin secretes from visceral fat and in blood its shows insulin – mimetic effects which correlate with a wide range of biologic effects including glucose and lipid metabolism and visfatin may be a promising biomarker for predicting obesity, insulin resistance, metabolic syndrome, diabetes mellitus, cardiovascular diseases and cancer (4). On the other hand, some studies had reported no association between visfatin and diabetes.

Tumor Necrosis Factor – α:

Tumor necrosis factor (TNF) is a classical, pleiotropic pro-inflammatory cytokine. It is also the first 'adipokine' described to be produced from adipose tissue, regulated in obesity and proposed to contribute to obesity-associated metabolic disease. Tumor necrosis factor alpha (TNF-α), also known as TNF superfamily member 2 (TNFSF2) or simply TNF, is a multifunctional cytokine that has well-established immunological roles in innate and adaptive immunity and in the normal physiological functions of immune cells, where its production and actions tend to be both temporally and spatially limited. By contrast, abnormally elevated and sustained production of TNF is associated with pathogenic inflammatory disease states including infection-linked sepsis and chronic autoimmune diseases. In recent decades, TNF has also come to be known as an adipokine, after the serendipitous observation of its elevated production in adipose tissue in obesity, which led to the appreciation of the inflammatory nature of obesity and associated metabolic pathologies. These and other critical observations stimulated the exponential growth in our understanding of adipose tissue biology and obesity and together fuelled a renaissance in the field of energy metabolism (5).

Fetuin-A:

Fetuin-A, also referred to as α2-Heremans–Schmid glycoprotein (AHSG), is a protein with pleiotropic metabolic effects secreted by the liver. In addition to being a hepatokine, fetuin-A has recently been described as a potential hepatokine since its expression and secretion levels have been also shown to be increased in visceral adipose tissue of obese animal models and humans with MetS (6). The association of its circulating levels with MetS is currently gaining importance in the literature as a novel biomarker and possible risk factor for the development of MetS. Fetuin-A mediates macrophage migration and infiltration into the adipose tissue by way of chemo-attractants, thus inducing inflammatory cytokine release and subsequently contributing to the development of MetS.

INSULIN RESISTANCE:

Insulin Resistance, identified as an impaired biological response to insulin stimulation of target tissues primarily involves liver, muscle and adipose tissue.

Insulin:

Insulin is a peptide hormone composed of 51 amino acids and has a molecular weight of 5808 Da. It is produced in the islets of langerhans in the pancreas. Insulin induces cells in the liver, muscle, and fat tissue to take up glucose from the blood, storing it as glycogen in the liver and muscle, and stopping use of fat as an energy source. Recent studies have mentioned that metabolic dysfunction is a key risk factor for obesity related cancer and weight gain is associated with 20-50% increase in the risk of diagnosis with an obesity associated tumor types and circulating plasma insulin concentrations have been shown to independently predict the risk of cancers in humans (7). Insulin resistance is a reduced physiological response of the peripheral tissues to the actions of insulin results in increased production of this hormone by the pancreas and ensuing hyperinsulinemia.

APOLIPOPROTEINS:

It is commonly accepted that Apolipoproteins influence the progression of obesity by a variety of mechanisms including lipid metabolism, energy expenditure and inflammatory response. The pathophysiology of MetS involves multiple mechanisms that are not yet not fully understood. Regardless of these mechanisms, they result in three major processes: hormonal activation, chronic inflammation and insulin resistance there is evidence of an association between apolipoprotein alterations and some of these mechanisms.

Apolipoprotein A1:

Apolipoprotein A1 is the major protein component of high density lipoprotein (HDL) in plasma, encoded by the APOA1 gene. The protein promotes cholesterol efflux from tissues to the liver for excretion. It is a cofactor for lecithin cholesterolacyltransferase (LCAT) which is responsible for the formation of most plasma cholesteryl esters. ApoA-I was also isolated as a

prostacyclin (PGI2) stabilizing factor, and thus may have an anti clotting effect (8). Several studies have revealed that decreased serum apoA1 concentrations elicit cholesterol accumulation in arterial wall cells and the early formation of atherosclerotic plaques.

Apolipoprotein B100:

Apolipoprotein B100 (APOB100) is the primary apolipoprotein of low-density lipoproteins (LDL or "bad cholesterol"), which is responsible for carrying cholesterol to tissues. High levels of APOB100 can lead to plaques that cause vascular disease (atherosclerosis), leading to heart disease. There is considerable evidence that levels of APOB100 are a better indicator of heart disease risk than total cholesterol or LDL. APOB100 reflects lipoprotein particle number (independent of their cholesterol content), and it is a determinant of atherosclerosis and heart disease, large numbers of LDL particles, lead to competition at the APOB100 receptor (i.e. LDL receptor) of peripheral cells. Since such a competition will prolong the residence time of LDL particles in the circulation, it may lead to greater opportunity for them to undergo oxidation and/or other chemical modifications (8).

AIMS AND OBJECTIVES:

- The aim of this study is to examine the serum levels of Adipokines,Hepatokine, Apolipoproteins and Insulin in overweight, obese adults with and without metabolic syndrome.
- To correlate the adipokines, hepatokine, apolipoproteins and insulin levels with other biochemical and anthropometric parameters in the study population.
- To correlate the anthropometric parameters, basic biochemical parameters like, FBS, Lipid Profile and Blood pressure with other adipokines, hepatokine, apolipoproteins and insulin

HYPOTHESIS/ RESEARCH QUESTIONS:

- What is the risk of metabolic syndrome and its associated complications in Indian overweight and obese population?
- This study is designed to assess the hypothesis that "Overweight and Obese individuals have more risk of developing metabolic syndrome and its associated complications, when compared to individuals with a normal healthy weight".

REVIEW OF LITERATURE:

Numerous studies have shown that obesity particularly central obesity is a risk factor for metabolic syndrome and metabolic syndrome has also been found to be associated with a 2 fold increased risk of cardiovascular mortality, type 2 diabetes mellitus and certain cancers such as endometrial, breast, ovarian, prostate, liver, gall bladder, kidney and colon (8). Adipokines are involved in angiogenesis, adipose tissue metabolism and inflammation and modulate tissue sensitivity for insulin. Studies have reported that chemerin is involved in the regulation of adipocyte differentiation and therefore may have a primary role in the pathogenesis of obesity & obesity related disorders including inflammation and metabolic syndrome (2). Chemerin might clinically serve as a marker for body composition and it is tightly corresponded to changes in body weight. Recent reviews and epidemiological studies have implicated that adipocytes are responsible for storing excess calories as triglycerides and also provide strong evidence to energy imbalance that leads to adipocyte hypertrophy and hyperplasia and increase intracellular lipids, proinflammatory cytokines and circulating free fatty acids which are the risk factors involved in the pathogenesis of dyslipidemia (6).

Visfatin is secreted from visceral fat and its blood shows insulin – mimetic effects which correlate with a wide range of biologic effects including glucose and lipid metabolism. visfatin may be a promising biomarker for predicting obesity, insulin resistance, metabolic syndrome, diabetes mellitus, cardiovascular diseases and cancer. Visfatin may play role in the

pathogenesis of diabetes through interaction with the insulin receptor and it phosphorylates tyrosine and insulin substrate 1 and 2 (9).

Fetuin-A contributes to the etiology of Insulin Resistance (IR) by inhibiting insulin receptor tyrosine kinase activity. Obesity and insulin resistance interact in the development of type 2 diabetes on the tissue-specific effects of fetuin inhibition on the human insulin receptor tyrosine kinase or alternative pathway may shed new light on the regulatory mechanisms behind dyslipidemia, hypertension, and abnormal glucose metabolism (5). Fetuin-A is additionally responsible for promoting lipid-induced insulin resistance by the enhancement of free fatty acids binding to toll-like receptor 4 (TLR4) through an endogenous ligand function mediated by its terminal galactoside moiety, which is able to directly bind the Leu100–Gly123 and Thr493–Thr516 residues in TLR4,leading to adipose tissue inflammation and subsequent onset of insulin resistance. It is suggested that high fetuin-A levels can cause peripheral arterial disease (PAD). On the other hand, lower fetuin-A levels were associated with higher CVD risk in individuals without diabetes. Previous epidemiological studies showed an independent association between fetuin-A and IR and future development of diabetes mellitus in general population. The fetuin-A expression among different tissues is controversial. Earlier investigations have revealed that fetuin-A majorly involved in physiological and cellular metabolisms like fatty acid and protein metabolisms, bone metabolism, calcium homeostasis and regulation of inflammation (10).

TNF-α is the first proinflammatory cytokine recognized for its involvement in pathogenesis of insulin resistance and T2DM. It has been reported that TNF-α reduces the expression of insulin-regulated glucose transporter type 4 (GLUT4) which is located mainly in adipocytes and skeletal and cardiac muscles. In obese T2DM patients, the TNF-α plasma level is related to the amount of visceral fat and is not instantly affected in poorly controlled diabetic patients by acute lowering of blood glucose level. Patients with MetS had significantly greater serum

IL-6 and TNF-α levels than the controls, supporting the evidence that inflammation plays an important role in the immune pathogenesis of the disease. Additionally, TNF-α serum levels may predict MetS. Interestingly, elevated serum TNF-α levels are associated with MetS independent of MetS components (11).

Patients with Type 2 diabetes mellitus or the metabolic syndrome have unique dyslipidemia characterized by hypertriglyceridemia; elevated blood levels of apolipoprotein B100, small dense low-density lipoprotein (LDL) cholesterol and low levels of high-density lipoprotein (HDL) cholesterol. Apolipoprotein A-1 is more important than the HDL cholesterol content for biochemical pathways that make HDL anti-atherogenic (7).

Apo lipoprotein B levels also provide a good measure of the number of LDL particles which reflects the atherogenicity of LDL. Collectively, these considerations have led to recommendations to implement the apolipoprotein B/A-1 ratio in routine clinical care in improving lipoprotein-related cardiovascular risk prediction. Regarding insulin resistance, numerous studies have established correlation between ApoA1, Apo B and ApoA1/ApoB ratio with insulin resistance in both diabetic and normo-glycemic patients. However, the association between lipoproteins and insulin resistance appears to be a two-way relationship. This is due to the suggestion that under conditions of insulin resistance, the inhibitory effect of insulin on lipase activity is diminished, resulting in increased free fatty acids release through lipolysis. This, in turn, can lead to modifications in atherogenic lipoproteins, including the overproduction of ApoB. It is worth emphasising that some authors consider the ApoB/ApoA1 ratio as the most accurate marker for assessing the balance between atherogenic and anti-atherogenic lipoproteins (12).

Early identification and treatment of Met S components are essential for the prevention and reduction of cardiovascular events and T2DM. However, traditional lipid biomarkers cannot provide sufficient accuracy in the measurement of dyslipidemia. Alongside, transporting

molecules like apolipoprotein B (ApoB) are present in all atherogenic types of lipoproteins such as low-density lipoprotein cholesterol (LDL-C), very low density lipoprotein cholesterol (VLDL-C), and intermediate-density lipoproteins (IDL), and their determination enables a more precise estimation of atherogenicity than the conventional lipid profile. ApoA1 is considered a favored alternative to HDL-C in the prediction of cardiovascular diseases, insulin resistance and DM (12).

A reduction in insulin signaling primarily in the insulin receptor substrate (IRS)/ phosphoinositide-3-kinase (PI-3K)/protein kinase B (PKB) axis triggers insulin resistance that could affect the metabolic actions of insulin. Insulin resistance is commonly linked with obesity, which is a pathophysiologic factor of type 2 diabetes mellitus (T2DM).In addition, insulin resistance and hyperinsulinemia can contribute to the development of obesity (13).

Several studies found fasting hyperinsulinaemia and insulin resistance to be risk factors for weight gain in later years. Studies in adults do not offer consistent results. Over the past 2 decades, it has been recognized that obesity is associated with chronic lowgrade inflammation in a variety of tissues, including adipose tissue (AT), skeletal muscle, liver, pancreas islet, intestine, and even brain. Both innate and adaptive immune cells can participate in obesity-linked inflammation, which, importantly, may serve as a causal link between obesity and insulin resistance and T2DM (8).

METHODOLOGY:

A cross-sectional study consists of 200 subjects with in the age group of 20-70 years. Subjects attended Medicine OPD at Tomo Riba Institute of Health & Medical Sciences, Naharlagun, Arunachal Pradesh were enrolled as study participants. A detailed questionnaire recorded the medical history of all the participants. This study was approved by the Institutional Ethics Committee. Written Informed consent form from all the participants was

obtained before the commencement of the study. The experimental design consisted of 4 Groups.

Group-I:(N=50)

This group consisted of healthy controls (BMI between 18.5 and 24.9 kg/m^2) without any clinical evidence for any disease.

Group-II:(N=50)

This group consisted of only overweight (BMI between 25 and 29.9 24.9 kg/m^2) without any clinical evidence for any disease.

Group-III:(N=50)

This group consisted of obesity (BMI above 30 24.9 kg/m^2) without any clinical evidence for any disease.

Group-IV:(N=50)

This group consisted of obesity with metabolic syndrome. Subjects with metabolic syndrome were identified using the IDF criteria. These criteria define metabolic syndrome as having central obesity (waist circumference >90 cm in men, and >80 cm in women) along with two of the following factors: 1) TG 150 mg/dL or higher 2) HDL levels < 40mg/dL in men or < 50 mg/dL in women 3) BP 130/85 mmHg or higher, and 4) fasting blood glucose > 100 mg/dL.

Exclusion Criteria:

1. Adults with secondary causes of obesity such as Cushing's syndrome, polycystic ovary syndrome, hypogonadism, hypothyroidism, and drugs induced obesity were excluded.
2. Adults with known history of diabetes, cardiovascular diseases, cancer and relevant drug treatment were excluded.

3. Adults undergoing treatment for any other comorbid conditions were excluded.

Inclusion Criteria:

1. Adults with age range between 20 to 70 years were included.
2. Healthy Controls were included.
3. Adults with Overweight were included.
4. Adults with Obesity were included.
5. Obese adults with Metabolic syndrome as per IDF criteria were included.

Statistical Analysis:

Sample size was calculated (by a qualified statistician from the Sri Balaji Vidyapeeth University) assuming alpha=0.001, beta = 0.1 (power =90%)

$$\frac{2\sigma^2(Z_{1-\beta}+Z_{1-\alpha/2})^2}{(\mu_1-\mu_2)^2}$$

Statistical analysis of the data was done by using SPSS version 23.0;SPSS Inc;Chicago IL, USA. Descriptive analysis the categorical variable were analyzed by using frequency and percentages and the continuous variables were analyzed by calculating Mean ± SD, for inferential analysis the numerical data were analyzed using the "t" test and correlation, the categorical data were analyzed using "Chi square test". Correlation analysis was done by Pearson correlation coefficient at 5% level of significance.

Collection of Blood Samples:

Routine Biochemical, Anthropometric Parameters and Clinical Parameters:

- Venous blood samples were collected after 12 hour fasting from all the subjects.
- Serum separated and the samples were stored at -20^{0}c until analysis.

- Lipid profile which includes Total Cholesterol (TC), Low Density Lipoprotein – Cholesterol (LDL-C), High Density Lipoprotein – Cholesterol (HDL-C) were analyzed by enzymatic method using fully autoanalyzer (Agappe). Serum Triglycerides (TG) by GPO-PAP method.
- Fasting Glucose levels were analyzed by GOD-POD method using fully autoanalyzer (Agappe) all the samples for lipid profile and fasting glucose were analyzed immediately.
- Anthropometric measurements such as height, weight, body mass index (BMI), waist to hip ratio (WHR) and Neck Circumference (NC) were recorded. Weight was measured using a beam balance to the nearest 0.1kg and height was measured to the nearest centimeter using a tape stuck to the wall. Abdominal girth was measured at the level of umbilicus with the subject relaxed and in a standing posture. Hip girth was measured at the widest point of the hips at the level of the greater trochanter with the subject standing with both feet together. Waist to hip ratio was calculated from these measurements. Neck circumference was measured in the midway of the neck between mid cervical spine and mid-anterior neck to within 1mm using non stretchable plastic tape with subjects standing upright in men with a laryngeal prominence, it was measured just below the prominence.
- Blood pressure levels were also recorded for all the subjects using a mercury sphygmomanometer.

Adipokines:

Serum Chemerin was measured by ELISA Kit (Finetest Company)

Serum visfatin was measured by ELISA Kit (Finetest Company)

Serum TNF-Alpha was measured by ELISA Kit (Abbkine Company)

All the adipokines were measured by using Alere AM2100 ELISA Reader.

Hepatokine:

Serum Fetuin-A was measured by ELISA Kit (Finetest Company) by using Alere AM2100 ELISA Reader.

Insulin Resistance:

Serum Insulin was measured by ELISA Kit (Diametra Company) by using Alere AM2100 ELISA Reader.

Homeostasis Model Assessment (HOMA-IR) calculated by following formula.

HOMA-IR = fasting insulin (μU/ml) × fasting glucose (m mol/L)/22.5.

Apolipoproteins:

Apolipoprotein A-I & Apolipoprotein B was estimated by Turbidometric Immuno Assay (Diasys company) using BeneSphera C 61.

Apo-B/Apo-AI ratio calculated by following formula.

Apo-B/Apo-AI ratio = Apo-B (mg/dl) / Apo-AI (mg/dl).

RESULTS AND DISCUSSIONS:

Table 1: Comparison of descriptive and clinical characteristics between different groups

Parameter	**Group 1 (Healthy controls)**	**Group 2 (Overweight)**	**Group 3 (Obese without metabolic syndrome)**	**Group 4 (Obese with metabolic syndrome)**
	Mean±SD	**Mean±SD**	**Mean±SD**	**Mean±SD**
Age(yrs)	41.5±13.4	37.1±10.9 †	40.6±12.7 †	42.0±9.2 †
BMI(kg/m2)	21.5±1.8	27.2±1.2**	31.4±1.9**	32.8±2.7**
WHR	0.8±0.1	0.8±0.1 †	0.9±0.0**	0.9±0.1**
Neck Circumference	14.1±0.8	14.6±0.7*	15.8±1.0**	16.2±1.1**
Glucose (mg/dL)	90.2±8.8	95.2±10.7*	94.9±8.5*	108.5±10.4**

Total cholesterol (mg/dL)	167.5±32.3	177.1±37.7 ŧ	190.4±26.8*	219.6±42.3**
Triglycerides (mg/dL)	121.9±33.0	162.8±68.1*	150.2±41.2**	242.0±96.1**
HDL-C(mg/dL)	48.8±11.6	43.2±9.1*	49.1±6.2 ŧ	40.6±7.0*
LDL-C (mg/dL)	92.2±26.2	104.3±36.1 ŧ	107.5±22.4*	135.0±40.5**
VLDL(mg/dL)	24.1±6.8	32.5±13.6*	29.8±8.2**	48.0±18.8**
APO A1(mg/dL)	125.2±18.6	120.1±12.5 ŧ	117.1±14.5*	117.1±18.1 ŧ
APO B100(mg/dL)	90.3±19.9	114.4±29.2**	121.7±24.6**	137.8±26.9**
APO B/APO A1 Ratio	0.7±0.2	1.0±0.3**	1.1±0.3**	1.2±0.4**
SBP(mmHg)	116.2±6.4	117.6±5.6 ŧ	117.8±6.8 ŧ	133.8±10.7**
DBP(mmHg)	79.6±6.7	79.4±5.5 ŧ	79.8±6.8 ŧ	87.8±8.2**
Chemerin (ng/mL)	0.7 ± 0.5	2.0 ± 0.4**	4.7 ± 2.6**	7.6 ± 1.0**
Visfatin (ng/mL)	1.0 ± 0.2	1.7 ± 0.3**	4.3 ± 3.2**	10.9± 6.6**
Fetuin-A(ng/mL)	1.9 ± 0.8	5.5 ± 1.2**	10.7 ± 2.1**	32.9 ± 10.5**
Insulin(µIU/mL)	4.7±3.0	10.8±0.8**	14.2±2.4**	20.3±6.3**
TNF-α (pg/mL)	21.7±11.8	128.5±35.7**	171.5±13.6**	238.6±62.0**
HOMA-IR	1.04±0.6	2.53±0.38**	3.33±0.67**	5.41±1.6**

** p<0.001, * p<0.005, ł p>0.05

BMI – Body Mass Index, WHR – Waist to Hip Ratio, NC – Neck Circumference

TC – Total Cholesterol, TG – Triglycerides, HDL-C – High Density Lipoprotein-Cholesterol, LDL-C – Low Density Lipoprotein- Cholesterol, VLDL – Very Low Density Lipoprotein, S.B.P – Systolic Blood Pressure, D.B.P – Diastolic Blood Pressure.

Table 2: Comparison between the male and female participants from the different groups.

Parameter	**Group l (Healthy controls)**	**Group 2 (Overweight)**	**Group 3 (Obese without metabolic syndrome)**	**Group 4 (Obese with metabolic syndrome)**

	Males (N= 17)	**Females(N= 33)**	**Males(N= 13)**	**Females(N= 37)**	**Males(N= 16)**	**Females(N= 34)**	**Males(N= 23)**	**Females(N= 27)**
Age(yrs)	42.1±12.7	41.1±13.9	37.6±12.2	36.8±10.6	42.1±10.8	39.8±13.5	41.5±9.1	42.3±9.5
BMI(kg/m2)	21.7±1.7	21.3±1.7	27.0±1.2**	27.2±1.1**	30.8±1.2**	31.7±2.1**	33.1±3.3**	32.5±1.9**
WHR	0.78±0.06	0.78±0.06	0.8±0.07†	0.81±0.06†	0.86±0.05**	0.86±0.04**	0.88±0.05**	0.87±0.04**
Neck Circumference	14.6±0.69	13.8±0.74	14.9±0.65†	14.5±0.68*	16.4±1.0**	15.4±0.87**	16.4±1.0**	15.9±1.0**
Glucose (mg/dL)	88.8±8.0	90.8±9.2	95.7±15.1†	95.0±8.8†	96.6±11.6†	93.9±6.5†	108.2±9.8**	108.7±11.0**
Total cholesterol (mg/dL)	164.6±37.5	168.9±29.7	166.9±40.4†	180.6±36.5†	183.1±25.8†	193.8±26.9**	223.0±41.0**	216.6±43.9**
Triglycerides (mg/dL)	120.6±34.3	122.5±32.7	171.7±61.9*	159.6±70.6*	137.8±18.2*	156.0±47.5**	261.1±132.1**	225.6±45.1**
HDL-C(mg/dL)	48.5±11.6	48.9±11.7	41.3±6.5†	43.8±9.8†	47.0±3.4†	50.1±6.9†	39.3±7.1**	41.7±6.7**
LDL-C (mg/dL)	87.4±29.7	94.5±24.2	93.6±33.6†	107.9±36.6†	103.5±25.5†	109.3±20.9*	139.9±38.1**	130.7±42.5**
VLDL(mg/dL)	24.0±6.9	24.1±6.8	34.2±12.3*	31.8±14.1*	27.3±3.6†	30.9±9.4*	51.5±25.8**	45.0±9.0**
APO A1(mg/dL)	123.5±12.4	126.0±21.2	123.0±11.6†	119.0±12.7†	115.1±16.3†	118.0±13.7†	119.7±17.9†	114.7±18.3†
APO B100(mg/	89.5±16.6	90.6±21.5	99.5±19.2†	119.5±30.4**	122.8±25.7**	121.2±24.3**	140.7±31.7**	135.2±22.3**

dL)								
APO B/APO A1 Ratio	0.73±0.15	0.73±0.21	0.82±0.22[ł]	1.0±0.26**	1.09±0.31**	1.05±0.28**	1.22±0.40**	1.21±0.31**
SBP(mm Hg)	118.2±8.0	115.1±5.0	116.9±6.3[ł]	117.8±5.3[ł]	119.3±6.8[ł]	117.0±6.7[ł]	135.2±1.6**	132.5±9.8**
DBP(mm Hg)	78.2±6.3	80.3±6.8	79.2±4.9[ł]	79.4±5.7[ł]	80.0±6.3[ł]	79.7±7.1[ł]	88.2±10.2**	87.4±5.9**
Chemerin (ng/mL)	0.73±0.41	0.69±0.42	2.15±0.34**	1.96±0.47**	4.9±2.8**	4.6±2.5**	7.9±1.0**	7.4±1.1**
Visfatin (ng/mL)	0.95±0.20	1.0±0.19	1.76±0.33**	1.64±0.34**	4.6±3.9**	4.1±2.9**	11.5±6.8**	10.4±6.4**
Fetuin-A(ng/mL)	1.91±0.78	1.89±0.76	5.7±1.6**	5.4±1.3**	10.7±2.5**	10.6±1.8**	34.1±10.2**	31.8±10.7**
Insulin(μIU/mL)	4.3±2.8	4.92±3.0	10.7±0.81**	10.7±0.83**	15.2±3.0**	13.7±1.8**	18.5±5.9**	21.8±6.1**
TNF-α (pg/mL)	24.6±23.0	20.2±19.3	136.2±34.8**	125.8±36.0**	170.5±12.1**	171.9±14.3**	245.0±74.0**	233.0±50.2**
HOMA-IR	0.92±0.59	1.07±0.67	2.54±0.45**	2.52±0.32**	3.62±0.87**	3.19±0.52**	4.88±1.4**	5.85±1.76**

** $p<0.001$, * $p<0.005$, ł $p>0.05$

BMI – Body Mass Index, WHR – Waist to Hip Ratio, NC – Neck Circumference

TC – Total Cholesterol, TG – Triglycerides, HDL-C – High Density Lipoprotein-Cholesterol, LDL-C – Low Density Lipoprotein- Cholesterol, VLDL – Very Low Density Lipoprotein, S.B.P – Systolic Blood Pressure, D.B.P – Diastolic Blood Pressure

ADIPOKINES:

Chemerin:

The results of this study demonstrate elevated levels of serum chemerin in overweight, obese with and without metabolic syndrome. The available information strongly suggests that

chemerin is essential in early differentiation process and may contribute to or regulate critical early events in adipogenesis and metabolic homeostasis and also indicates that chemerin could have an important biological role in the formation of white adipose tissue during normal development and in pathological states such as obesity and our data agree with those reported by others (14). However previous studies have produced mixed results some revealed opposite or no association. Within this study we observed unfavourable lipid profile and higher odds of dyslipidemia. Serum chemerin showed positive correlations with anthropometric parameters, visfatin, fetuin-A, TNF-α, insulin, Apo B, TC, TG, LDL-C & VLDL. Furthermore, serum chemerin levels positively correlated with both Systolic Blood Pressure (SBP) & Diastolic Blood Pressure (DBP). Our results revealed the inverse association between chemerin concentration and Apo A1, HDL-C. Collectively, the findings presented above provide strong evidence to energy imbalance leads to adipocyte hypertrophy and hyperplasia and moreover to increase intracellular lipids, proinflammatory cytokines and circulating free fatty acids which are the risk factors involved in the pathogenesis of dyslipidemia.

Visfatin:

The present study shows elevated levels of serum visfatin in overweight, obese with and without metabolic syndrome. In contrast, one study has shown less visfatin in obesity.Taken together the present findings suggests that visfatin is synthesized and released by inflammatory cells in adipose tissue as well as adipocytes and subclinical inflammation in overweight and obesity may have enhanced expression of visfatin. In similar way by others current study findings also suggest that inflammation is a condition which sits at the very base of atherogenesis, which is the major consequence of the metabolic syndrome and adipose tissue impacts all organs by the synthesis of adipokines (15). Visfatin levels positively correlated with anthropometric parameters, chemerin, fetuin-A, TNF-α, insulin,

Apo B, TC, TG, LDL-C, VLDL and Blood pressure. While the association between visfatin concentration and Apo A1, HDL-C was negative. Fasting glucose levels were significantly elevated in overweight, obese with and without metabolic syndrome and we found positive correlation between visfatin and fasting glucose. The present study findings strongly suggest that visfatin influences the glucose metabolism, may be plasma visfatin levels are related to progressive β cell deterioration and increased insulin resistance possibly mediates the link of the adipocytokine with diabetes and visfatin can be stimulated under a hyperglycemic environment. Visfatin may play role in the pathogenesis of diabetes through interaction with the insulin receptor and it phosphorylates tyrosine and insulin substrate 1 and 2(16).

TNF-α:

In the present study, we show elevated levels of serum TNF-α in overweight, obese with and without metabolic syndrome and our results are in alignment with the earlier reports. In contrast, few studies have not shown significant elevation of TNF-α in overweight and obesity. Our observations suggest that increased inflammatory cytokines lead to the persistence of inflammation in obese subjects. TNF can impair insulin receptor signalling in adipocytes by stimulating endoplasmic reticulum Ca^{2+} release, increasing cytosolic free Ca^{2+} levels and activating Ca^{2+} calmodulin-dependent protein kinase II (CamKII) .These events are mediated in part by a JNK-dependent increase in inositol triphosphate receptor (IP3R) Ca^{2+} channels. These observations raise the possibility that CamKII involvement in the downregulation of insulin-stimulated glucose uptake and the link between gene variants of IP3R and 'metabolically healthy' obesity. Taken together our data suggests that TNF-α abnormalities in the inflammatory state associated with obesity and the dysregulated production of inflammatory mediators have critical roles in multiple co-morbidities of obesity (17). Serum TNF-α showed positive correlations with anthropometric parameters, fasting glucose, chemerin, visfatin, fetuin-A, Apo B,TC, TG, LDL-C & VLDL. While the

association between TNF-α concentration and Apo A1, HDL-C was negative. Our findings strongly suggest that TNF-α is mediated in part by stimulation of hepatic lipid synthesis and adipose lipolysis along with suppression of triacylglycerol clearance and inhibition of insulin stimulated de novo lipogenesis in adipose tissue and elevation of TNF-α in obesity may directly promote the development of cardiovascular risk.

HEPATOKINE:

Fetuin-A:

The results of this study showed increased levels of serum fetuin-A in overweight adults and obese adults with and without metabolic syndrome. The available information strongly suggests that fetuin-A is involved in the decrease in lipogenesis and increase in lipolysis in the adipose tissue thereby stimulating obesity and insulin resistance. We hypothesized that liver might influence body energy homeostasis by governing the glucose and lipid metabolism and our data are consistent with those reported by other studies. It is generally believed that elevated fetuin-A levels in obesity with metabolic syndrome is a significant predictive factor for type 2 diabetes and myocardial infarction/stroke (18). Furthermore, the serum fetuin-A levels were positively correlated with anthropometric, biochemical parameters and both SBP and DBP and inverse association is observed with Apo A1 & HDL-C. Our observations imply that fetuin-A and metabolic syndrome have a functionally relevant association with obesity and play a pivotal role in the pathophysiology of metabolic disease.

INSULIN RESISTANCE:

In the present study, we show elevated levels of serum insulin and HOMA-IR in overweight, obese with and without metabolic syndrome. Insulin levels positively correlated with anthropometric parameters. Emerging evidence and our own observations suggest that insulin receptor is commonly expressed in tumors. In addition, Insulin receptor binding activates the insulin receptor substrate/phosphoinositide 3-kinase/Akt cascade, which ultimately promotes

activation of the mammalian target of rapamycin complex (mTORC). mTORC signaling clearly plays a role in cancer cell proliferation via control of transcription, ribosome biogenesis, protein synthesis, angiogenesis, and autophagy and may participate in Warburg metabolism. Therefore, a shift from oxidative to glycolytic metabolism allowing cancer cells to remain alive despite low perfusion/oxygenation, fueled by anaerobic metabolism of glucose to pyruvate, generating large quantities of lactate by reduction of lactate to regenerate NAD+, which is consumed during glycolysis. mTORC2 activity upregulates the expression of pyruvate kinase M isozyme-1 (PKM1), a constitutively active enzyme that converts phosphoenolpyruvate to pyruvate, thereby catalyzing – along with its conditionally activated counterpart, PKM2 – the final step in glycolysis. PKM1 was recently shown to promote tumor cell survival, highlighting an important permissive role for PKM1 regulation of glycolysis. Serum insulin levels are positively correlated with anthropometric parameters, chemerin, visfatin, fetuin-A, TNF-α, Apo B,TC, TG, HOMA-IR, LDL-C & VLDL. While the association between TNF-α concentration and Apo A1, HDL-C was negative. Taken together our data suggest that HOMA-IR is associated with obesity and hyperinsulinemia both are established risk factors for cancers (19).

APOLIPOPROTEINS:

The present study data shows lower serum Apolipoprotein A1 levels in Overweight, Obese without metabolic syndrome and Obese with metabolic syndrome than in control. Serum Apolipoprotein B100 levels was significantly higher in Overweight, Obese without metabolic syndrome and Obese with metabolic syndrome than in control. Apo B/Apo A ratio was significantly higher in Overweight, Obese without metabolic syndrome and Obese with metabolic syndrome than in control. Our data strongly suggest that apolipoproteins are predictive factor for metabolic syndrome independent of the components of metabolic syndrome and apolipoproteins are one of the effective risk factors for predicting CVD and

Type 2 DM and our results are in agreement with the previous studies reported. Serum Apolipoprotein A1 levels negatively correlated with anthropometric parameters such as BMI, WHR,NC and biochemical parameters such as glucose,chemerin,visfatin,fetuin-A,TNF-α, Apo B100, TC, TG, LDL-C and both SBP, DBP. Whereas positively correlated with HDL-C. The present study findings indicate that role of visceral fat in HDL metabolism in obesity and the concept that low HDL-C in obesity may be associated with apoA1 degradation and impaired cholesterol efflux from lipoprotein and cellular sources, their higher risk of developing coronary heart disease and our findings are in alignment with earlier reports. Serum Apolipoprotein B100 levels positively correlated with anthropometric parameters, biochemical parameters and negatively correlated with Apo A1 and HDL-C. Our findings strongly suggest that the number of metabolic syndrome components were an independent predictive factor for apo B100, probably in metabolic syndrome where insulin resistance plays an important role would be considered to have a correlation with apo B100 (20).

SUMMARY AND CONCLUSIONS:

- The present study observed elevated adipokines, hepatokine, insulin resistance markers and abnormal apolipoproteins in overweight, obese with and without metabolic syndrome when compared with healthy controls. Positive correlations were noticed between Adipokines (Chemerin, Visfatin, TNF-α), Hepatokine (Fetuin-A), Apolipoprotein B100, Insulin with anthropometric parameters, lipid profile and B.P(both systolic and diastolic) furthermore, our results revealed the inverse association with Apo A1 and HDL-C. Serum Apolipoprotein A1 levels negatively correlated with anthropometric parameters, biochemical parameters. Whereas positively correlated with HDL-C.

- The current data belief is that chemerin is involved in the regulation of adipocyte differentiation and it may have a primary role in the pathogenesis of obesity & obesity related disorders including inflammation and metabolic syndrome.
- These finding implies that visfatin is synthesized and released by inflammatory cells in adipose tissue as well as adipocytes and subclinical inflammation in overweight and obesity may have enhanced expression of visfatin and inflammation is the major consequence of the metabolic syndrome.
- The hypothesis of this study is that elevated fetuin-A levels in overweight and obesity with and without metabolic syndrome can influence various metabolic processes and play a pivotal role in inflammation. Obesity particularly central obesity is the prominent risk factor for insulin resistance, metabolic syndrome, type 2 diabetes mellitus, cardiovascular diseases and cancer.
- TNF-α is produced by both immune and non immune cells within minutes of any injury or stress by pro-inflammatory stimuli. It is quite evident that TNF-α levels increases in obesity, metabolic syndrome independent of metabolic syndrome components. It is directly associated with insulin resistance. Our findings reinforce the notion that elevated TNF-α in overweight and obesity may be a promising biomarker for predicting insulin resistance, diabetes mellitus, metabolic syndrome, cardiovascular diseases and cancer.
- Our study emphasizes the complex relationship between obesity, insulin function, and the likelihood of developing cancer. Increased levels of insulin in the blood, disrupted processing of fats, and measurements related to the size and shape of the body have been identified as important factors in the advancement of cancer.
- Our data strongly suggest that apolipoproteins are predictive factor for metabolic syndrome independent of the components of metabolic syndrome and apolipoproteins

are one of the effective risk factors for predicting CVD and Type 2 DM. Apo B/Apo A1 ratio well characterizes the dyslipidemia associated metabolic syndrome and it is the accurate marker for assessing the balance between atherogenic and anti atherogenic lipoproteins and independently predict subsequent myocardial infarction.

- Therefore, a correct understanding of the pathogenesis of obesity is the prerequisite for guiding the formulation of obesity prevention and treatment strategies. Diagnosis of metabolic syndrome at an early stage is important to employ lifestyle and risk factor modification. This study highlights the importance of chemerin, visfatin, TNF-α and Fetuin-A biomarker measurement in overweight and obese subjects for the early prediction of metabolic syndrome and its associated complications. Furthermore, the future research on larger sample size should endeavor to elucidate the exact mechanism of adipokines and hepatokine etc., in overweight and obesity.

ABSTRACT:

Background: There is compelling evidence that in every region the number of people living with obesity is more than underweight. Obesity particularly central obesity is a risk factor for metabolic syndrome and metabolic syndrome has also been found to be associated with a 2 fold increased risk of cardiovascular mortality, type 2 diabetes mellitus and certain cancers.

Aims & Objectives: To evaluate Adipokines, Heptokine, Apolipoproteins, Insulin and its correlation with anthropometric, biochemical and blood pressure in overweight, obese with and without metabolic syndrome and healthy controls.

Methods: The serum levels of Adipokines, Heptokine and Insulin measured by using ELISA and Apolipoproteins by Immunoturbidimetry and basic biochemical parameters by using fully autoanalyzer in 200 subjects (50 Healthy Controls, 50 Overweight, 50 Obese without metabolic syndrome and 50 Obese with metabolic syndrome as per IDF criteria) of age group 20-70 years.

Results: The levels of serum adipokines, hepatokine, insulin and Apo B100 elevated and positively correlated with other biochemical anthropometric and clinical parameters In contrary, Apo A1 and HDL-C decreased in overweight and obese with and without metabolic syndrome.

Conclusion: Adipokines, hepatokine, and insulin is associated with metabolic diseases. they controls the entire energy homeostasis of the body probably by regulating glucose and lipid metabolism. The current data belief is that Adipokines, hepatokine may be a promising biomarker for predicting metabolic syndrome and its associated disorders particularly in overweight and obese adults.

Keywords: Adipokines, Hepatokine, Insulin, Apolipoproteins, Obesity, Metabolic syndrome

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CONFERENCES ATTENDED:

1. Presented Paper titled" Clinical Significance of Serum Tumor Necrosis Factor-Alpha (TNF-α) Levels in Obese and Patients with Metabolic Syndrome" organized by the Department of Biochemistry, College of Medicine & JNM Hospital, WBUHS in association with Association of Clinical Biochemists of India & Indian Immunology Society between 27-29th March 2024.
2. Presented Paper titled" Insulin Resistance in Obesity:an Unexplored Angle" organized by the Department of Biochemistry, College of Medicine & JNM Hospital, WBUHS in association with Association of Clinical Biochemists of India & Indian Immunology Society between 27-29th March 2024.

PAPERS PUBLISHED/ACCEPTED:

1. Sruti Eswar, Balaji Rajagopalan, Kenyi Ete, Srinivasa Nageswara Rao Gattem. Exploring Insulin Resistance in Obesity: A Cross-Sectional Study from Arunachal Pradesh. Afr.J.Bio.Sc. 2024;6(8):2692-10.
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Original Article

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Biochemistry Section

Visfatin as an Early Marker for the Diagnosis of Metabolic Syndrome in Obese Adults: A Cross-sectional Study

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ABSTRACT

Introduction: It is well-established that obesity plays a significant role in the development of metabolic syndrome. Visfatin is a novel adipocytokine predominantly secreted in adipose tissue, associated with a wide range of biological effects including glucose and lipid metabolism. Visfatin levels are significantly linked to inflammation and the development of obesity-related metabolic disorders. Unfortunately, the roles of visfatin in obesity, particularly in the Indian population, are scarce.

Aim: To study the role of serum visfatin in diagnosing metabolic syndrome in overweight and obese adults.

Materials and Methods: A comparative cross-sectional study was conducted at the Department of Biochemistry, Tomo Riba Institute of Health and Medical Sciences, Naharlagun, Arunachal Pradesh, India, between September 2022 and October 2023. A total of 200 subjects (50 controls, 50 overweight individuals, 50 obese individuals without metabolic syndrome, and 50 obese individuals with metabolic syndrome), aged 20-70 years, were enrolled as study participants. Anthropometric parameters, lipid profiles, and fasting glucose were analysed using an auto analyser. Serum visfatin levels were measured by Enzyme-linked Immunosorbent Assay (ELISA). Statistical analysis was performed using the t-test, and categorical data were analysed using the Chi-square test. Correlation analysis was done by Pearson's correlation at a significance level of 5%.

Results: The control group consisted of 17 males and 33 females with a mean age of 41.5±13.4 years, the overweight group consisted of 13 males and 37 females with a mean age of 37.1±10.9 years, the obese without metabolic syndrome group consists of 16 males and 34 females with a mean age of 40.6±12.7 years, and obese with metabolic syndrome group had 23 males and 27 females with a mean age of 42.0±9.2 years. Serum visfatin levels (ng/mL) were significantly elevated in the overweight (1.7±0.3), obese without metabolic syndrome (4.3±3.2), and obese with metabolic syndrome (10.9±6.6) groups compared to the controls (1.0±0.2). Serum visfatin levels were positively correlated with Body Mass Index (BMI) ($r=0.51$, $p<0.001$), Waist to Hip Ratio (WHR) ($r=0.41$, $p<0.001$), Neck Circumference (NC) ($r=0.50$, $p<0.001$), Fasting glucose ($r=0.44$, $p<0.001$), Total Cholesterol (TC) ($r=0.41$, $p<0.001$), Triglycerides (TG) ($r=0.39$, $p<0.001$), Low-Density Lipoprotein-cholesterol (LDL-c) ($r=0.39$, $p<0.001$), Very Low-Density Lipoprotein (VLDL) (VLDL) ($r=0.39$, $p<0.001$), Systolic Blood Pressure (SBP) ($r=0.52$, $p<0.001$), and Diastolic Blood Pressure (DBP) ($r=0.45$, $p<0.001$), and negatively correlated with High-Density Lipoprotein-cholesterol (HDL-c) ($r=-0.20$, $p<0.002$).

Conclusion: The present study revealed a good relationship between serum visfatin and the anthropometric and biochemical parameters. The current data belief is that visfatin may be a promising biomarker for predicting metabolic syndrome and its associated disorders particularly in overweight and obese adults.

Keywords: Body fat, Enzyme-linked immunosorbent assay, Lipid profile, Obesity

INTRODUCTION

There is now evidence from many studies that overweight and obesity have reached epidemic proportions globally, and perhaps India is undergoing a rapid epidemiological transition from underweight to an overweight/obese population [1,2]. Epidemiological studies have described that the prevalence of men and women living with overweight/obesity is observed to be 38.4% and 36.2%, respectively [3,4]. The Indian National Family Health Survey-4 reported that in the 10-year period from 2005 to 2006 to 2015 and 2016, obesity among women between the ages of 15 and 49 years increased from 13% to 21%. During the same period, obesity among men between the ages of 15 and 49 years increased from 9.3% to 19% [5]. Recent reports suggest that obesity is one of the most neglected public health problems and is also associated with unemployment, social disadvantages, and reduced socio-economic productivity [6].

The medical literature abounds with evidence that obesity, particularly central obesity, is a risk factor for metabolic syndrome. Metabolic syndrome has also been found to be associated with a 2 fold increased risk of cardiovascular mortality, type 2 diabetes mellitus, and certain cancers such as endometrial, breast, ovarian, prostate, liver, gall bladder, kidney, and colon [7,8]. Recently, an elegant study revealed that the prevalence of metabolic syndrome has dramatically increased in India. It has been found that the overall pooled prevalence of metabolic syndrome among the adult population was 30% [9].

It is commonly accepted that adipose tissue is an endocrine organ that produces molecules with important functions in the human body called adipokines. Visfatin is a recently discovered adipocytokine with a 55-kDa protein consisting of 491 amino acids, previously called Pre-β cell Colony Enhancing Factor (PBEF). Visfatin is secreted by macrophages (CD 14+) in visceral adipose tissue induced by hypoxia [10,11]. Under hypoxic conditions, hydroxylase processes are rendered inactive; consequently, hypoxia-inducible factor-1a is stabilised and moves into the nucleus where it binds to hypoxia response elements within target genes and initiates the transcription of visfatin [12,13].

Visfatin is synthesised and released by inflammatory cells in adipose tissue as well as adipocytes [11]. It has the ability to activate human leukocytes, induce the synthesis of proinflammatory cytokines and adhesion molecules, regulate the maturation of leukocytes B, and inhibit apoptosis of neutrophils [14]. Visfatin was first discovered by Fukuhara A et al., as an adipokine, and it has been stated that visfatin is secreted from visceral fat only and its blood shows insulin-mimetic effects [10]. Recent studies have mentioned that visfatin production is not limited to visceral fat alone and it is expressed and secreted in many other tissues such as adipose tissue, chondrocytes, heart,

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Serum Tumor Necrosis Factor Alpha (TNF-α) Levels in Obese and Overweight Adults: Correlations With Metabolic Syndrome and Inflammatory Markers

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Abstract

Background: Overweight and obesity are escalating public health concerns globally, and India is also experiencing a significant rise in the population of overweight and obese people. Tumour necrosis factor alpha (TNF-α) is a type of cytokine that has garnered attention in particularly obesity-related metabolic disturbances. This study aimed to assess TNF-α levels in overweight and obese adults and explore its correlation with metabolic syndrome and associated biochemical parameters in the northeastern Indian population.

Methods: A comparative study was conducted involving 200 participants divided into four groups: 50 healthy controls, 50 overweight individuals, 50 obese individuals without metabolic syndrome and 50 obese individuals with metabolic syndrome. Serum TNF-α levels were measured using the enzyme-linked immunosorbent assay (ELISA) method. Anthropometric measurements and biochemical analyses, including glucose and lipid profiles, were performed using standard methods.

Results: TNF-α levels were significantly elevated in overweight individuals (128.5±35.7 pg/ml), obese individuals without metabolic syndrome (171.5±13.6 pg/ml), and obese individuals with metabolic syndrome (238.6±62 pg/ml) compared to normal subjects (controls; 21.7±11.8 pg/ml). Positive correlations were observed between TNF-α and body mass index (BMI), waist-to-hip ratio (WHR), neck circumference, glucose, cholesterol, triglycerides, and negative correlation was found high-density lipoprotein cholesterol (HDL-C).

Conclusion: Elevated TNF-α levels in overweight and obese individuals suggest its role in metabolic disturbances and immune activation within the adipose tissue. These findings underscore the importance of monitoring TNF-α as a potential biomarker for metabolic syndrome risk, highlighting the need for targeted interventions in the northeastern Indian population to mitigate the health impacts of obesity and associated metabolic disorders.

Categories: Hematology
Keywords: biomarkers, metabolic syndrome, obesity, overweight, serum tnf-α

Introduction

Body mass index (BMI), a widely recognized measure of weight status, is typically used for the classification of overweight and obesity. The World Health Organization (WHO) and other health organisations classify weight as underweight, moderate, severe, or very severe. Other definitions include waist circumference (WC) and waist-to-hip ratio (WHR). Overweight is defined as having a WC of 94 cm or more for men and 80 cm or more for women, while obesity is defined as having a WC of 102 cm or more for men and 88 cm or more for women. Body fat percentage is also a measure of body fat. We use lower BMI thresholds in Asian populations to account for variations in body composition and related risk factors. Other factors when diagnosing overweight and obesity include age, gender, muscle mass, body fat distribution, and obesity-related health problems. These definitions are supported by reputable sources and studies emphasising regional variations and clinical factors [1-3]. Overweight and obesity have emerged as significant global public health challenges, with ample data suggesting a shift of the population in India from underweight to overweight and obesity, known as an epidemiological transition. Epidemiological research indicates that those with overweight or obesity have a 38% higher prevalence compared to those who do not have these conditions. The particular prevalence rates for individuals with overweight and obesity are 4% and 36.2%, respectively [1]. The Indian National Family Health Survey conducted in 2015-16 revealed a significant surge in obesity rates among females aged 15-49, increasing from 13% in 2005-2006 to 21%. In the same age range, there was a corresponding increase in the occurrence of obesity among males, rising from 9% to 19% [2].

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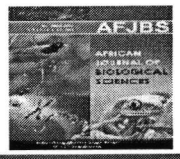

Research Paper

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Exploring Insulin Resistance in Obesity: A Cross-Sectional Study from Arunachal Pradesh

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Dear Dr. G:

It is a pleasure to accept your manuscript entitled "The Clinical and Biochemical parameters in relation to Serum Fetuin – A levels in Overweight and Obese with and without Metabolic syndrome in North-Eastern states of Indian Population." in its current form for publication in the JMA Journal. The comments of the reviewer(s) who reviewed your manuscript are included at the foot of this letter.

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